

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.: 10/786,907
Filing Date: February 25, 2004
Applicant: Bjarne Bogen
Group Art Unit: 1643
Examiner: BRISTOL, Lynn Anne
Title: Modified Antibody
Attorney Docket: 36731S-000001/US

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Pre-Appeal Brief Request for Review Accompanying a Notice of Appeal

Sir:

In response to the Final Office Action of July 1, Applicants have filed a Notice of Appeal. Before preparing an appeal brief, Applicants request a pre-appeal brief review of the Examiner's rejections. This Request is accompanied by a Notice of Appeal and the fee for filing a Notice of Appeal. With a two month extension, reply is timely on December 1, 2011.

Remarks begin on page 2 of this paper.

REMARKS

Claims 83, 88-92, 98-100, 119, 121 and 123 stand rejected as obvious over Herman, US 2005/0069549, published March 31, 2005, filed Jan 14, 2003; cited in the PTO 892 form of 11/7/06 (“*Herman*”) in view of Slavin-Chiorini et al. Int. J. Can. 53:97-103 (1993) (“*Slavin*”). Applicants request review of any rejection remaining after the entry of the final amendment. In particular, Applicants traverse the obviousness rejection as discussed below.

Contrary to the Examiner’s stated position, the combined references do not contain all of the claim features arranged as presented in the claims.

The holding of obviousness gives improper weight to Applicants’ arguments as presented in the After Final Amendment of September 1, 2011. The primary reference *Herman* does not present a dimeric molecule having features arranged as in the claims. Accordingly, even if the secondary *Slavin* is used to provide a missing feature (that the dimer lacks a CH2 domain), the result does not lead to the claimed subject matter.

As discussed in the September 2011 Amendment, the claims recite an isolated nucleic acid encoding a monomer unit of a homodimeric molecule consisting of an antigenic unit (AU), a dimerization motif (DM) and a targeting unit (TU). The DM consists of an Ig hinge region and a Cγ3 region. *Herman* teaches an antibody-type molecule, but does not specifically teach a nucleic acid encoding a monomer with a TU and an AU separated by a DM. See pages 14-15 of the September 2011 Amendment for a discussion of the deficiencies of *Herman* in this regard.

In the claimed invention, the DM does not include a CH2 domain. *Slavin* discloses mouse antibodies lacking a CH2 domain. The rejection is then based on combining *Herman* and *Slavin* for the latter’s “teaching” of removing a CH2 domain. But combining the references in this way ignores the other deficiencies of the primary reference. Applicants request reversal of the rejection on the grounds that the references, even when combined, still do not contain all of the claim elements arranged as in the claims.

Even if all the elements were to be found in the cited references, the skilled artisan would not have combined the references, for the reasons of record.

Despite the deficiencies of *Herman*, the Examiner concludes that, because *Slavin* teaches the exclusion of a CH2 domain, the claimed nucleic acid is obvious over *Herman* in light of *Slavin*. But this position is held against a preponderance of evidence supporting the opposite conclusion.

In the Amendment of April 2011, Applicants discussed the incompatible teaching of *Slavin* And *Herman*, noting that the Examiner appreciated the premise of the argument, i.e. that the two references present incompatible goals with respect to the question of serum half-lives. Attention is drawn to pages 13-17 of the April 2011 Amendment, including Applicants' summary of the argument:

Simply put, it is not predictable that an immunotherapy based on the targeted ligand provided by *Herman* would actually benefit by making a CH2-deprived antibody, as per [Slavin].

Applicants' position was repeated in the September 2011 Amendment.

Applicants provided further evidence of non-obviousness, which they urge has been given insufficient weight. A declaration by E. Sally Ward, Ph.D. accompanied the 10/26/10 reply to the Examiner's 6/1/10 Final Office Action. Ward holds a Ph.D. in Biochemistry and Molecular Biology from the University of Cambridge, England, and is currently a professor (with an endowed title) of Molecular Immunology at the University of Texas Southwestern Medical Center in Dallas, Texas. She had performed research concerning molecular immunology for about 20 years at the time of the declaration, and has an impressive record of publishing immunology articles in peer-reviewed journals. Upon reviewing Applicants' claims and the prior art references, Dr. Ward declared:

It is my position that a person of ordinary skill in the art would not combine and modify the Herman document in view of the Slavin-Chiorini document because Herman refers to prolonged serum half-life as desirable, and consequently a skilled artisan would not turn to Slavin-Chiorini in order to modify the Herman disclosure to decrease the half-life of the multispecific ligand.

It is Ward's contention that, since *Herman* deals with immunotherapy where a prolonged serum half-life is desirable, and since *Slavin* relates to clinical diagnosis with a radioisotope where a long serum half-life is not desirable, the two references are antagonistic and so would not be combined by a person of ordinary skill in the art.

For the aforementioned reasons, the Examiner's *prima facie* showing of obviousness has been rebutted by a preponderance of evidence. Because independent claim 83 is for that reason not obvious from the cited combination of art, each of the rejected dependent claims is patentable for the same reasons.

Accordingly, Applicants respectfully request withdrawal of the rejections and allowance of the claims.

CONCLUSION

Applicants have completed their response to the final rejection by filing a Notice of Appeal of even date with this Pre-Appeal Brief Request For Review. Based on the above discussion, the obviousness rejection is wrongly applied against the amended claims. Further and favorable consideration is solicited. If the Examiner or the review panel believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1278.

Respectfully submitted,

Dated: December 1, 2011

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